

What is claimed is:

1. A polypeptide comprising in order from the N-terminus to the C-terminus:

- a) a prodomain comprising at least six contiguous amino acids of SEQ ID NO:3;
- b) an engineered cleavage site; and
- c) a protease domain;

wherein the polypeptide is capable of being cleaved at the engineered cleavage site thereby releasing a free protease domain that has BACE activity.

2. The polypeptide of claim 1 wherein the engineered cleavage site is an autoproteolysis site.

3. The polypeptide of claim 1 wherein the engineered cleavage site is an exogenous protease cleavage site.

4. A polypeptide comprising in order from the N-terminus to the C-terminus:

- a) a prodomain comprising SEQ ID NO:3;
- b) an autoproteolysis site comprising the sequence X1-X2-X3-X4-X5,
wherein

X1 is Glu or Gln,

X2 is Leu, Ile or Val,

X3 is Asn, Asp or Met,

X4 is Leu or Phe, and

X5 is Glu, Met, Gln, Ser, Ala or Asp; and

- c) a protease domain comprising at least 20 contiguous amino acids from residues 74-446 of SEQ ID NO:1;

wherein the polypeptide is capable of being cleaved at the autoproteolysis site thereby releasing a free protease domain that has BACE activity.

5. The polypeptide of claim 4 wherein the protease domain comprises at least one sequence

selected from the group consisting of SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, and SEQ ID NO:55.

6. The polypeptide of claim 4 wherein the protease domain comprises at least 60 contiguous amino acids from residues 74-446 of SEQ ID NO:1.
7. The polypeptide of claim 4 wherein the protease domain comprises at least 120 contiguous amino acids from residues 74-446 of SEQ ID NO:1.
8. The polypeptide of claim 4 wherein the protease domain comprises at least 180 contiguous amino acids from residues 74-446 of SEQ ID NO:1.
9. The polypeptide of claim 4 wherein the protease domain comprises residues 74-446 of SEQ ID NO:1.
10. The polypeptide of claim 4 wherein the autoproteolysis site is selected from the group consisting of:
 - a) ELNLETD (SEQ ID NO:56),
 - b) EINLETD (SEQ ID NO:57),
 - c) EINFETD (SEQ ID NO:58), and
 - d) EVNLDAE (SEQ ID NO:59).
11. The polypeptide of claim 4 wherein the autoproteolysis site is selected from the group consisting of:
 - a) EINFSEFVE (SEQ ID NO:60),
 - b) EINFQFVD (SEQ ID NO:61), and
 - c) EINFSEASF (SEQ ID NO:62).
12. The polypeptide of claim 4 wherein the prodomain comprises residues 22-41 of SEQ ID NO:1.
13. The polypeptide of claim 4 wherein the prodomain comprises residues 22-45 of SEQ ID NO:1.

14. A polypeptide comprising an amino acid sequence that is at least 85% identical to residues 22-446 of SEQ ID NO:1 wherein the sequence includes at least one autoproteolysis site X1-X2-X3-X4-X5,

wherein

X1 is Glu or Gln,

X2 is Leu , Ile or Val,

X3 is Asn, Asp or Met,

X4 is Leu or Phe, and

X5 is Glu, Met, Gln, Ser, Ala or Asp.

15. The polypeptide of claim 14 wherein the amino acid sequence is at least 90% identical to residues 22-446 of SEQ ID NO:1.

16. The polypeptide of claim 14 wherein the amino acid sequence is at least 95% identical to residues 22-446 of SEQ ID NO:1.

17. A polypeptide comprising an amino acid sequence at least 85% identical to residues 22-446 of SEQ ID NO:1 wherein the sequence includes

a) a subsequence that is at least 90% identical to residues 74-446 of SEQ ID NO:1; and

b) at least one autoproteolysis site X1-X2-X3-X4-X5,

wherein

X1 is Glu or Gln,

X2 is Leu , Ile or Val,

X3 is Asn, Asp or Met,

X4 is Leu or Phe, and

X5 is Glu, Met, Gln, Ser, Ala or Asp; and

wherein X1 is located at least 6 residues from the N-terminus of the sequence.

18. A nucleic acid sequence encoding the polypeptide of claim 1.

19. A vector for expression of the polypeptide of claim 1.

20. A host cell expressing the polypeptide of claim 1.